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REVIEW ARTICLE

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Risk factors for surgical site infection in patients with gastric cancer: A meta-analysis

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Abstract

Surgical Site Infection (SSI) is one of the common postoperative complications after gastric cancer surgery. Previous studies have explored the risk factors (such as age, diabetes, anaemia and ASA score) for SSI in patients with gastric cancer. However, there are large differences in the research results, and the correlation coefficients of different research results are quite different. We aim to investigate the risk factors of surgical site infection in patients with gastric cancer. We queried four English databases (PubMed, Embase, Web of Science and the Cochrane Library) and four Chinese databases (China National Knowledge Infrastructure, Chinese Biological Medicine Database, Wanfang Database and Chinese Scientific Journal Database (VIP Database)) to identify published literature related to risk factors for surgical site infection in patients with gastric cancer. Rev Man 5.4 and Stata 15.0 were used in this meta-analysis. A total of 15 articles ($n = 6206$) were included in this analysis. The following risk factors were found to be significantly associated with surgical site infection in gastric cancer: male (OR = 1.28, 95% CI [1.06, 1.55]), age >60 (OR = 2.75, 95% CI [1.65, 4.57]), smoking (OR = 1.99, 95% CI [1.46, 2.73]), diabetes (OR = 2.03, 95% CI [1.59, 2.61]), anaemia (OR = 4.72, 95% CI [1.66, 13.40]), preoperative obstruction (OR = 3.07, 95% CI [1.80, 5.23]), TNM ≥ III (OR = 2.05, 95% CI [1.56, 2.70]), hypoproteinemia (OR = 3.05, 95% CI [2.08, 4.49]), operation time ≥3 h (OR = 8.33, 95% CI [3.81, 18.20]), laparotomy (OR = 2.18, 95% CI [1.61, 2.94]) and blood transfusion (OR = 1.44, 95% CI [1.01, 2.06]). This meta-analysis showed that male, age >60, smoking, diabetes, anaemia, preoperative obstruction, TNM ≥ III, hypoproteinemia, operation time ≥3 h, open surgery and blood transfusion were the risk factors for SSI in patients with gastric cancer.

Muxin Chen and Hao Liang contributed equally to this work.

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KEYWORDS

gastric cancer, meta-analysis, risk factors, surgical site infection

Key Messages

- this is a meta-analysis to investigate the risk factors of surgical site infection in patients with gastric cancer
- male, age >60, smoking, diabetes, anaemia, preoperative obstruction, TNM ≥ III, hypoproteinemia, operation time ≥3 h, laparotomy operation and blood transfusion were identified as risk factors for the development of SSI after surgical operation of gastric cancer patients, with low heterogeneity between results. the funnel plot and Egger's test of sex as a risk factor show no significant publication bias among pooled studies
- our findings provided much stronger and more sufficient evidence to identify and evaluate the risk factors for SSI after gastric cancer surgery

1 | INTRODUCTION

Gastric cancer (GC) is one of the most common gastrointestinal malignancies in the world. According to data from the Global Cancer Epidemiology Database (GLOBOCAN) in 2020, there were about 1 089 000 cases and 769 000 deaths of gastric cancer in the world, with a global incidence of 5.6% and a mortality rate of 7.7%.[1] Currently, surgical operation is still the primary treatment for gastric cancer.[2] Surgical Site Infection (SSI) is one of the most common postoperative complications after gastric cancer operation, as well as one of the most common nosocomial infections with an incidence of about 30%.[3,4] The occurrence of SSI can result in a prolonged postoperative hospital stay and increased medical costs, affecting postoperative rehabilitation and the quality of life of patients.[5,6] Thus, it is very important to identify and treat the perioperative risk factors to reduce the occurrence of SSI in patients with gastric cancer.

Previous studies have explored the risk factors for SSI in patients with gastric cancer. However, there are large differences in the research results, and the correlation coefficients of different research results are quite different. For example, Kosuga et al. reported that male gender and chronic liver disease were independent risk factors for SSI in gastric cancer patients after surgery, whereas diabetes, anaemia, ASA score and hypoproteinemia were not associated with SSI.[7] In other previous studies,[8,9] ASA score, diabetes, smoking and duration of surgery were associated with SSI. The exact factors associated with SSI in patients with gastric cancer and the correlation coefficients between them remain unclear. Therefore, this study aimed to examine the risk factors of SSI among gastric cancer patients as valuable information for developing better interventions and management of gastric cancer.

2 | METHODS

This study was registered to the international database of prospective registered systematic reviews (PROSPERO) with registration number CRD42022322277. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[10]

2.1 | Search strategy

We queried four English databases (PubMed, Embase, Web of Science and the Cochrane Library) and four Chinese databases (China National Knowledge Infrastructure, Chinese Biological Medicine Database, Wanfang Database and Chinese Scientific Journal Database (VIP Database)) to identify published literature related to risk factors for surgical site infection in patients with gastric cancer from the date of each database's inception up to December 2022. The main keywords were "stomach neoplasms" or "gastric cancer" or "gastric neoplasms" and "surgical wound infection" or "surgical site infections" and "risk factors" or "influence factors" or "dangerous factors." The PubMed search strategy is provided in Data S1.

2.2 | Eligibility criteria

We included studies that met the following conditions: (1) all gastric cancer patients with surgical treatment were included; (2) SSI diagnostic criteria are derived from Diagnostic Criteria for Nosocomial Infection or Centres for Disease Control and Prevention criteria;[11,12] (3) the case and control groups were defined according to the presence or absence of SSI after surgery of gastric cancer;

(4) the risk factors related to SSI were reported; (5) the study design consisted of case–control study, cohort study, or other observational studies.

The following studies were excluded during screening: (1) with the risk factors for other types of infections, such as postoperative anastomotic fistula, pulmonary infection, abdominal infection and nosocomial infection; (2) published in a language other than English or Chinese; (3) studies on data errors, incomplete or unable to obtain full text; (4) duplicated studies and non-primary studies (i.e., meetings, review articles and editorials) and (5) the level of the New Castle-Ottawa Scale scores ≤4.

2.3 | Quality assessment

We evaluated the overall quality of case–control studies and cohort studies using the New Castle-Ottawa Scale (NOS). The evaluation contents include study population selection, inter-group comparability and outcome/exposure factor measurement. The level of scores ≤4, 5–6 and ≥7 was graded as low quality, moderate quality and high quality.[13]

2.4 | Study selection and risk of bias assessment

To address the risk of bias, two researchers (M.X.C. and M.Y.C.) independently assessed all the titles and abstracts to remove articles that obviously did not meet the study criteria. The studies that met the eligibility criteria were included for further evaluation with a full-text review. Data extraction from the accepted trials included: first author, year of publication, region of study, type of study, sample size and risk factors related to surgical site infection of gastric cancer. Differences of opinion were resolved by discussion between the two researchers. Two researchers (M.X.C. and M.Y.C) independently assessed the risk of bias of the New Castle-Ottawa Scale (NOS). Any disagreements were adjudicated by consulting a third author (L.W.)

2.5 | Statistical analysis

This meta-analysis was performed using RevMan 5.4 (Cochrane Collaboration) and STATA 15.0 (Stata Corp). Outcomes were presented as the odds ratios (ORs) with 95% confidence intervals (CIs). Heterogeneity across the studies was tested with the Q-test (test level $\alpha = 0.1$). The I^2 statistics were used as a quantitative measure of heterogeneity and the I^2 value of 25% to 50%, 50% to 75% and ≥75% was considered to indicate low heterogeneity, moderate heterogeneity and high heterogeneity, respectively.[14] A fixed-effects model was used if there was no significant heterogeneity ($P \geq .10$ and $I^2 \leq 50\%$); otherwise, a random-effects model was used. We

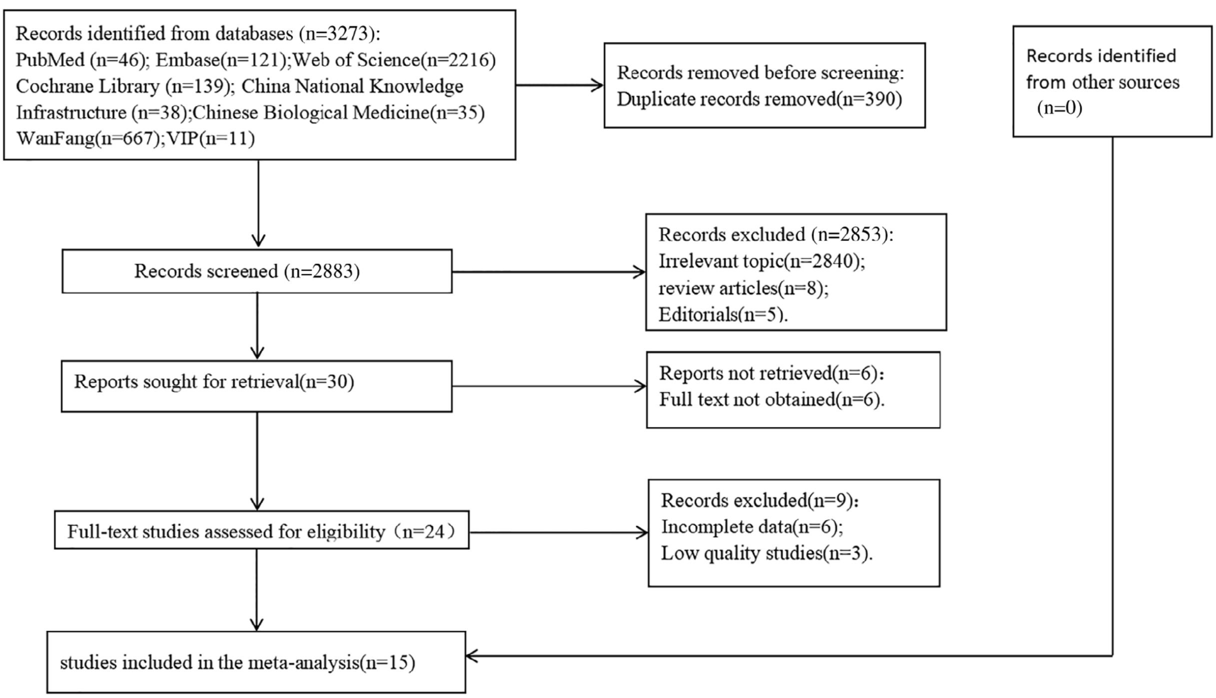

FIGURE 1 Flow chart of literature selection.

TABLE 1 Basic characteristics of the 15 included studies.

First author	Year	Country	Study design	Total (n)	SSI group (n)	SSI prevalence	Study population characteristics	Significant factors
Liu[16]	2012	China	Case–control	280	30	10.7%	Mean age: NA Range age: NA Gender: NA	③
Shi[25]	2013	China	Case–control	96	13	13.54%	Mean age: NA Range age: NA Gender: NA	⑪
Hirao[17]	2013	Japan	Case–control	355	24	7%	Mean age: NA Range age: 35 to 84 Gender Male: 240 (67.61%) Female: 115 (32.39%)	①
Hu[18]	2014	China	Case–control	412	39	9.47%	Mean age: 45.28 Range age: 27 to 76 Gender Male: 282 (68.45%) Female: 130 (31.55%)	①③⑧⑨
Dai[19]	2014	China	Case–control	492	97	19.72%	Mean age: 59.13 Range age: 26 to 79 Gender Male: 302 (61.38%) Female: 190 (38.62%)	①④⑤⑧⑬
Wang[20]	2015	China	Case–control	287	26	9.06%	Mean age: 51.7 Range age: 30 to 91 Gender Male:191 (66.55%) Female:96 (33.45%)	①②⑤⑧⑬
Endo[26]	2015	Japan	Case–control	685	42	6.1%	Mean age: NA Range age: 60 to 74 Gender Male: 484 (70.66%) Female: 201 (29.34%)	①
Yuji[21]	2017	Japan	Case–control	384	18	4.7%	Mean age: 67 Range age: 32 to 88 Gender Male: 264 (68.75%) Female: 120 (31.25%)	①⑩⑫
Xu[22]	2018	China	Case–control	410	50	12.0%	Mean age: 73 Range age: 65 to 92 Gender Male: 330 (80.49%) Female: 80 (19.51%)	①⑤⑥⑦⑨
Chen[27]	2018	China	Case–control	223	39	17.5%	Mean age: 61.5 Range age: NA Gender Male: 137 (61.43%) Female: 86 (38.57%)	①③④⑤⑨⑩⑫
Kim[23]	2019	Korea	Case–control	1038	58	5.6%	Mean age: 59 Range age: 50 to 67 Gender Male: 654 (63.00%) Female: 384 (37.00%)	①③④⑤⑧⑫

(Continues)

TABLE 1 (Continued)

First author	Year	Country	Study design	Total (n)	SSI group (n)	SSI prevalence	Study population characteristics	Significant factors
Kim[15]	2019	Korea	Cohort	353	25	7.1%	Mean age: 71 Range age: 67 to 75 Gender Male: 232 (65.72%) Female: 121 (34.28%)	①③④⑤⑥⑧⑨⑫
Ye[24]	2020	China	Case–control	160	38	23.75%	Mean age: NA Range age: >18 Gender Male: 110 (68.75%) Female: 50 (31,25%)	①④⑤⑩⑪⑫⑬
Gong[28]	2021	China	Case–control	180	90	50%	Mean age: 63.32 Range age: 45 to −79 Gender Male: 48 (26.67%) Female: 132 (73.33%)	①②⑤⑦⑩
Zhang[29]	2021	China	Case–control	851	79	9.28%	Mean age: 58.35 Range age: NA Gender Male: 548 (64.39%) Female: 303 (35.61%)	①④⑤⑥⑨⑩⑫

Abbreviations: ① sex; ② age>60; ③ smoking; ④ hypertension; ⑤ diabetes; ⑥ anaemia; ⑦Preoperative obstruction; ⑧ tumour lymph node metastasis (TNM) ≥ III; ⑨ hypoproteinemia; ⑩ ASA ≥ 3; ⑪ operation time ≥ 3 h; ⑫ surgery ways; ⑬ blood transfusion; NA, not available.

TABLE 2 Quality evaluation results of included studies in Meta-analysis of SSI risk factors in gastric cancer patients.

First author	Study population selection	Inter-group comparability	Outcome/exposure factor measurement	Total
Liu[16]	3	2	2	7
Shi[25]	3	1	2	6
Hirao[17]	3	2	2	7
Hu[18]	3	2	2	7
Dai[19]	3	2	2	7
Wang[20]	3	2	2	7
Endo[26]	3	1	2	6
Yuji[21]	3	2	2	7
Xu[22]	3	2	2	7
Chen[27]	3	1	2	6
Kim[23]	3	2	2	7
Kim[15]	4	2	2	8
Ye[24]	3	2	2	7
Gong[28]	3	1	2	6
Zhang[29]	3	1	2	6

performed a sensitivity analysis to assess the stability of the Meta-analysis results. A funnel plot and Egger's test were used to further determine the publication bias if there were a sufficient number of included trials (10 trials). $P < .05$ was considered significant.

3 | RESULTS

3.1 | Selection of studies

A total of 3273 articles were identified through our database search, of which 390 were duplicate studies. After reading the titles and abstracts, we excluded 2853 studies because the articles did not meet our eligibility criteria. After reading the full texts, 14 case–control studies and 1 cohort study were eligible for inclusion in this meta-analysis. All studies were published in English or Chinese between 2012 and 2021. In total, 6206 patients with surgical treatment were included in this analysis, including 668 patients with surgical site infections, and 13 contributing factors were extracted. The prevalence of SSI in all included studies was reported to vary between 4.7% and 50%. The outcome of quality assessment (NOS score) for these studies was as follows: one study scored 8[15]; nine studies scored 7[16-24]; five studies scored 6.[25-29] The selection process is presented in Figure 1. Detailed information about the included studies is shown in Tables 1 and 2.

3.2 | Effect of general factors on SSI

In this study, General factors included gender, age >60 and smoking. Low heterogeneity was observed between studies in terms of sex, age >60 and smoking ($I^2 \leq 50\%$, $P \geq .10$), so we used a fixed-effects model for meta-analysis. The meta-analysis results showed that the male (OR = 1.28, 95% CI [1.06, 1.55], $P = .01$), age >60 years

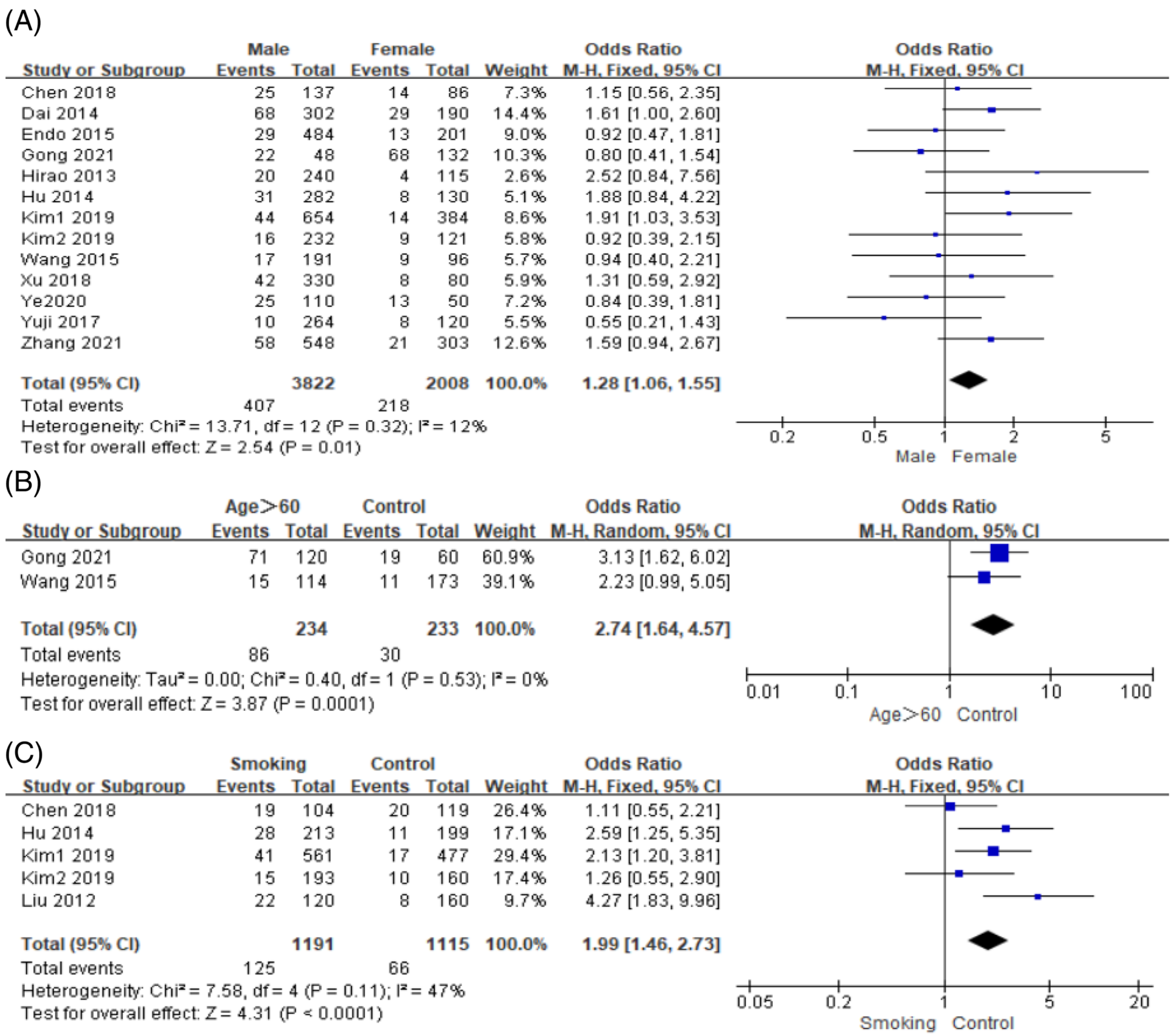

FIGURE 2 Forest plots of the meta-analysis of (A) sex, (B) age >60, (C) smoking.

old (OR = 2.75, 95% CI [1.65, 4.57], $P = .0001$), smoking (OR = 1.99, 95% CI [1.46, 2.73], $P < .0001$) were significant risk factors for SSI in gastric cancer. The forest plots of the meta-analysis are presented in Figure 2. The main outcomes of the meta-analysis are shown in Table 3.

3.3 | Effect of disease factors on SSI

In this study, the disease factors included hypertension, diabetes, anaemia, preoperative obstruction, TNM and hypoproteinemia. Among them, low heterogeneity was observed between studies in terms of hypertension, diabetes, preoperative obstruction, TNM and hypoproteinemia ($I^2 \leq 50\%$, $P \geq .10$), so we used a fixed-effects model for meta-analysis. Whereas moderate heterogeneity was observed between studies in terms of anaemia ($I^2 > 50\%$, $P < .10$), and the random-effects model was used for meta-analysis. On the basis of the pooled ORs and corresponding 95% CIs, the following risk factors were found to be significantly associated with SSI in gastric cancer:diabetes (OR = 2.03, 95% CI [1.59, 2.61], $P < .0001$), anaemia (OR = 4.72, 95% CI [1.66, 13.40], $P = .004$), preoperative obstruction (OR = 3.07, 95% CI [1.80, 5.23], $P < .0001$), TNM ≥ III (OR = 2.05, 95% CI [1.56, 2.70], $P < .0001$) and hypoproteinemia (OR = 3.05, 95% CI [2.08, 4.49], $P < .0001$). But no statistically significant difference was observed in terms of hypertension (OR = 1.24, 95% CI [0.94, 1.64], $P = .12$). The forest plots of the meta-analysis are presented in Figures 3 and 4, and the main outcomes of the meta-analysis are shown in Table 3.

3.4 | Effect of surgical operation factors on SSI

In this study, the surgical operation factors included ASA score, operation time, surgery ways and blood transfusion. Because low heterogeneity was observed between studies in terms of these factors ($I^2 \leq 50\%$, $P \geq .10$), we used a fixed-effects model for meta-analysis. The following risk factors were found to be significantly associated with SSI in gastric cancer: Operation time ≥ 3 h (OR = 8.33, 95% CI [3.81, 18.20], $P < .0001$), laparotomy (OR = 2.18, 95% CI [1.61, 2.94], $P < .0001$) and blood transfusion (OR = 1.44, 95% CI [1.01, 2.06], $P = .04$). ASA score was not significantly associated with SSI in gastric cancer (OR = 1.22, 95% CI [0.87, 1.72], $P = .25$). The forest plots of the meta-analysis are presented in Figure 5. The main outcomes of the meta-analysis are shown in Table 3.

3.5 | Sensitivity analysis results of risk factors

A sensitivity analysis was performed for risk factors (male, age >60 years, smoking, diabetes, anaemia, preoperative obstruction, TNM, hypoproteinemia, operation time ≥3 h, laparotomy and blood transfusion) by switching random and fixed effects models. The sensitivity analysis results showed that there was no statistical significance when the random-effects model was used for the blood transfusion factor (OR = 1.44, 95%

TABLE 3 The main outcomes of the meta-analysis.

Significant factors		No. of studies	I^2 (%)	Q test (P)	OR (95% CI)	P value
General factors	Sex	13[15,17-24,26-29]	12	0.32	1.28 (1.06, 1.55)	.01[a]
	Age > 60	2[20,28]	0	0.53	2.75 (1.65, 4.57)	.0001[a]
	Smoking	5[15,16,18,23,27]	47	0.11	1.99 (1.46, 2.73)	<.0001[a]
Diseases factors	Hypertension	6[15,19,23,24,27,29]	0	0.71	1.24 (0.94, 1.64)	.12[a]
	Diabetes	9[15,19,20,22-24,27-29]	12	0.33	2.03 (1.59, 2.61)	<.00001[a]
	Anaemia	3[15,22,29]	58	0.09	4.72 (1.66, 13.40)	.004[b]
	Preoperative obstruction	2[22,28]	0	0.99	3.07 (1.80, 5.23)	<.0001[a]
	TNM ≥ III	5[15,18–20,23]	24	0.26	2.05 (1.56, 2.70)	<.00001[a]
	Hypoproteinemia	5[15,18,19,22,27]	0	0.52	3.05 (2.08, 4.49)	<.00001[a]
Surgical operation factors	ASA ≥ 3	5[21,24,27–29]	0	0.78	1.22 (0.87, 1.72)	.25[a]
	Operation time ≥3 h	2[24,25]	0	0.39	8.33 (3.81, 18.20)	<.00001[a]
	Surgery ways	6[15,21,23,24,27,29]	0	0.74	2.18 (1.61, 2.94)	<.00001[a]
	Blood transfusion	3[19,20,24]	38	0.20	1.44 (1.01, 2.06)	.04[a]

Note: I^2 statistic was defined as the proportion of heterogeneity not due to chance or random error. The significance of statistics is shown in bold.
Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; OR, odds ratio; TNM, distant staging of local lymph node metastasis of primary tumour.
[a]Fixed-effects model was performed.
[b]Random-effects model was performed.

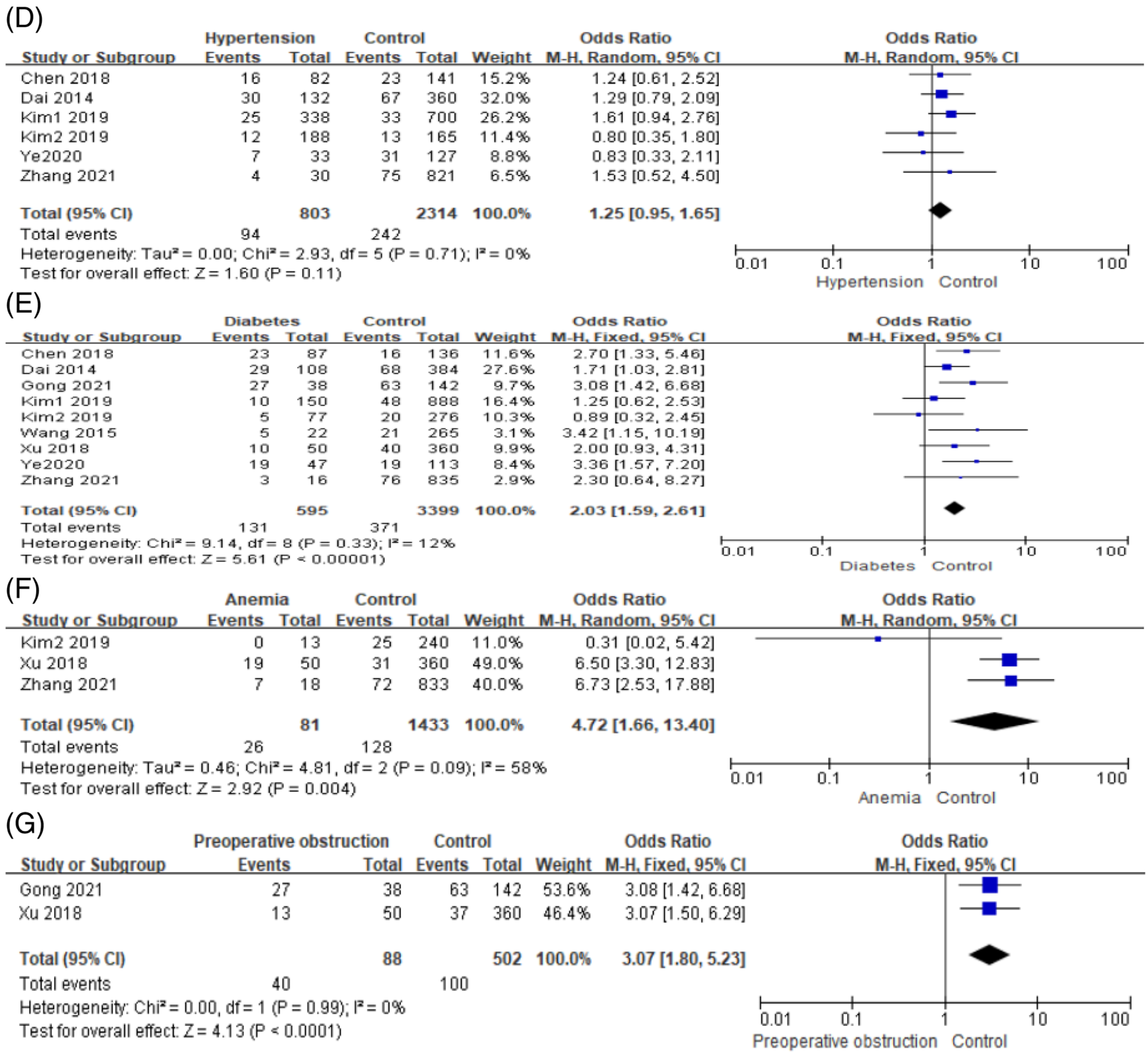

FIGURE 3 Forest plots of the meta-analysis of (D) hypertension, (E) diabetes, (F) anaemia, (G) preoperative obstruction.

CI [0.87, 2.37], $P = .16$), indicating the result was unstable. However, the meta-analysis results for other factors did not change the significance, indicating that the results were robust. The sensitivity results of meta-analyses are shown in Table 4.

3.6 | Evaluation of the publication bias

A total of 10 studies included data on sex factor, so we used the funnel plot and Egger's test to further determine the publication bias. The results showed that the *P* value was .634, indicating no publication bias on sex factor (Figures 6 and 7).

4 | DISCUSSION

This meta-analysis, including 15 articles with 6206 participants, showed that male, age >60, smoking, diabetes, anaemia, preoperative obstruction, TNM ≥ III, hypoproteinemia, operation time ≥3 h, laparotomy operation and blood transfusion were identified as risk factors for the development of SSI after surgical operation of gastric cancer patients, with low heterogeneity between results. Our findings provided much stronger and more sufficient evidence to identify and evaluate the risk factors for SSI after gastric cancer surgery.

In this meta-analysis, smoking, male and age >60 were found to significantly increase the risk of SSI.

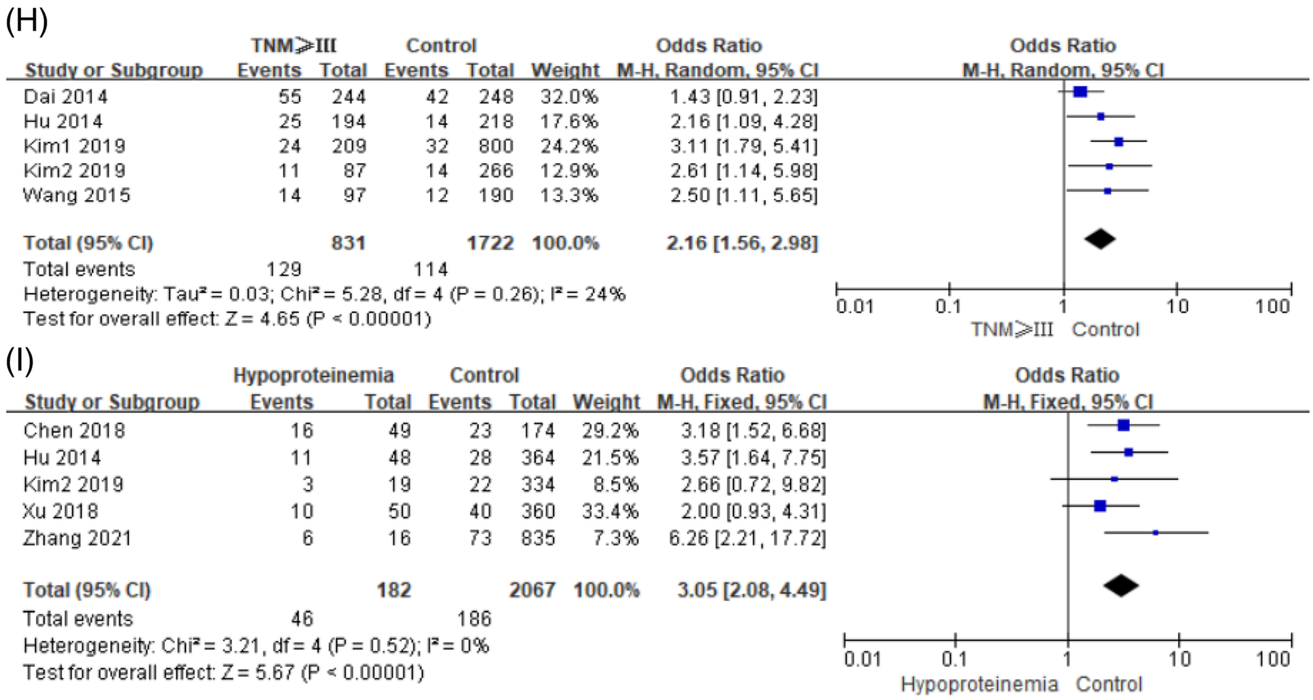

FIGURE 4 Forest plots of the meta-analysis of (H) tumour lymph node metastasis (TNM) ≥ III, (I) hypoproteinemia.

Smoking is currently recognised as one of the risk factors for SSI. Our results indicated that the risk of SSI was 1.99 times higher in smokers with gastric cancer than in non-smokers. A meta-analysis study of 500 000 patients[30] reported that smoking increased the incidence of SSI by 79% after surgery. A previous study reported that smoking could cause tissue hypoxia and hypoperfusion that led to the obstruction of nutrient transport and changes in the immune response, which would result in attenuated inflammatory response mechanisms and bactericidal mechanisms.[31] These reasons can cause poor wound healing and increase infection. Our results indicated that the risk of SSI was 1.28 times higher in men than in women, which may be associated with bad habits of daily life (such as smoking, drinking, etc.) in male gastric cancer patients, being consistent with Kosuga[7,21] but not with Hirao.[17] In addition, this study showed that age >60 was 2.75 times as likely to increase the risk of SSI in gastric cancer patients. In elderly patients, physiological functions of organs decline with age, and other chronic diseases are common, resulting in decreased immunity and anti-infection ability of the body, which may lead to an increased risk of SSI.[32-34] In perioperative management, it is notable that although gender and age are uncontrollable factors, more attention should be paid to elderly patients and male patients, and corresponding preventive measures should be given. Meanwhile, the patients should be advised to quit smoking early before surgery to reduce the occurrence of SSI.

Among the disease factors, our review showed that diabetes, anaemia, preoperative obstruction, TNM ≥ III and hypoproteinemia significantly increased the risk of SSI in patients with gastric cancer. In this study, the risk of SSI in gastric cancer patients with diabetes was 2.03 times higher than in non-diabetes patients, which was consistent with the previous study.[8] Martin et al. reported that diabetes was 1.53 times as likely to develop surgical site infections, and it also was an independent risk factor for SSI for multiple surgical procedure types.[35] For gastric cancer patients with diabetes, the phagocytosis and bactericidal ability of WBC were reduced due to a decrease in their own immunity and hyperglycemia, which resulted in the decreased anti-infection ability of patients and increased the opportunity of postoperative SSI.[20] In addition, abnormal blood glucose metabolism resulted in increased protein decomposition and decreased collagen synthesis, and the high blood glucose environment made it easy to breed bacteria, which prolonged postoperative wound healing time, led to an increased probability of SSI.[36] Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection recommended that it was necessary to implement perioperative glucose control and maintain blood glucose target levels less than 200 mg/dL in patients with and without diabetes.[37] A consensus report of the American College of Surgeons and Surgical Infection Society indicated that better short-term perioperative glycemic control (110–150 mg/dL) was important to lower the SSI risk.[38] Meanwhile,

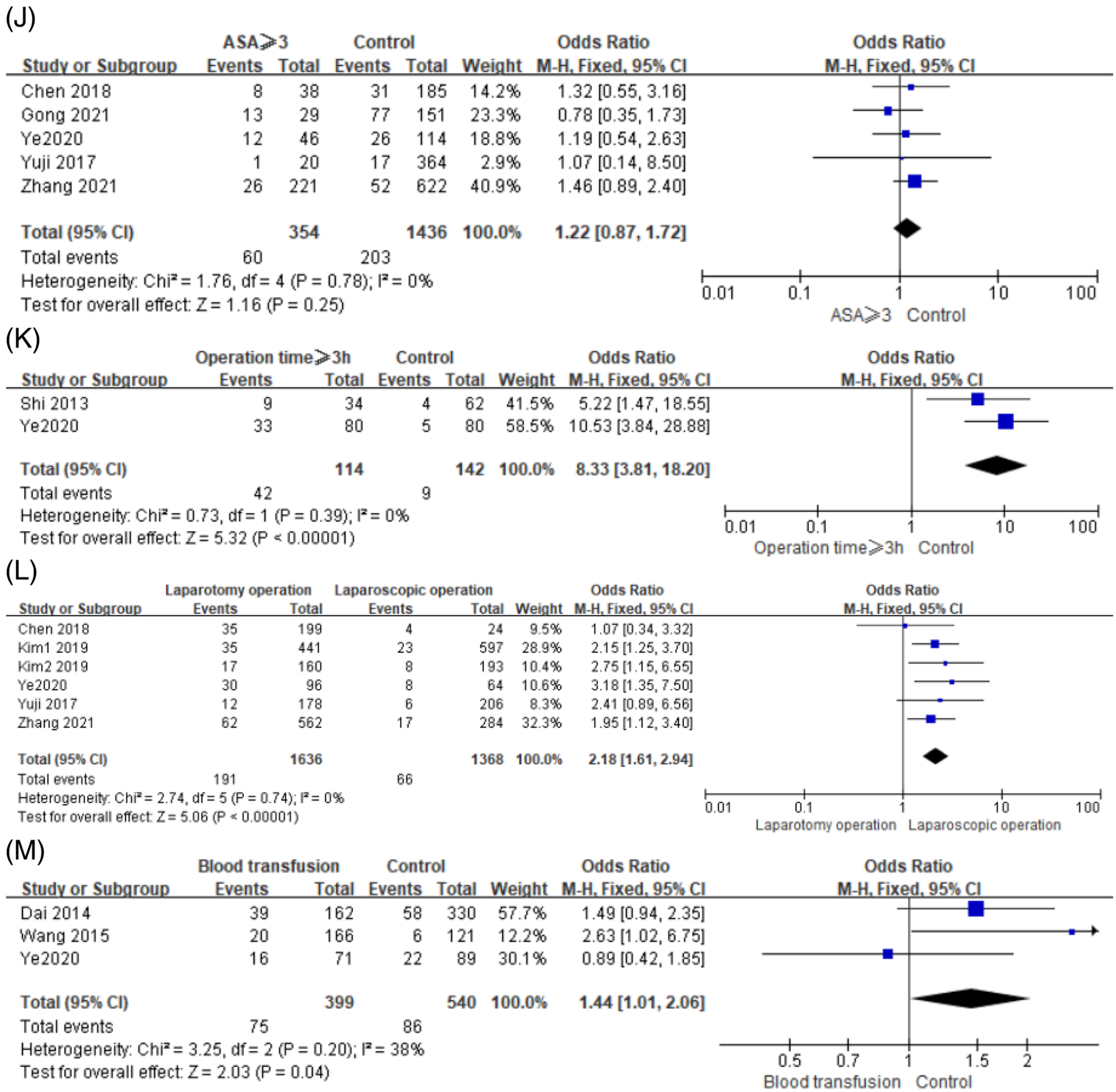

FIGURE 5 Forest plots of the meta-analysis of (J) ASA ≥ 3, (K) operation time ≥3 h, (L) surgery ways, (M) blood transfusion.

postoperative or intraoperative regulation combined with postoperative regulation of blood glucose could also significantly reduce the incidence of SSI.

Our results also indicated that anaemia, preoperative obstruction, TNM ≥ III and hypoproteinemia increased the risk of SSI in gastric cancer patients by 4.74 times, 3.07 times, 2.05 times and 3.05 times, respectively. Digestive and absorption disorders and long-term consumption of the disease may cause anaemia and hypoproteinemia and consequently raise malnutrition and reduce immune protein synthesis in patients with gastric cancer, resulting in inadequate surgical tolerance.[39] Weber et al. showed that anaemia (crude OR = 1.32, 95% CI [1.0, 1.7]) was significantly associated with an increased odds of SSI.[40] Patients with preoperative obstruction may have insufficient energy intake and malnutrition, which affect postoperative wound healing. In addition, the higher TNM stage was found to be associated with an increased risk of SSI. The higher the TNM stage, the greater the energy consumption of patients, which could raise the risk of malnutrition and decrease resistance of disease, resulting in increased difficulty of operation and prolonged operation time.[41] Chinese expert consensus on perioperative nutritional therapy for gastric cancer (2019 edition)[42] recommended that nutritional

Risk factors	Random-effects model OR (95% CI) *P*	Fixed-effects model OR (95% CI) *P*
Male	1.24 (1.01, 1.54) .04	1.28 (1.06, 1.55) .01
Age >60	2.74 (1.64, 4.57) .0001	2.75 (1.65, 4.57) .0001
Smoking	1.98 (1.27, 3.10) .003	1.99 (1.46, 2.73) <.0001
Diabetes	2.06 (1.56, 2.72) <.00001	2.03 (1.59, 2.61) <.00001
Anaemia	4.72 (1.66, 13.40) .004	4.74 (2.83, 7.94) <.00001
Preoperative obstruction	3.07 (1.81, 5.20) <.0001	3.07 (1.80, 5.23) <.0001
TNM ≥ III	2.16 (1.56, 2.98) <.00001	2.05 (1.56, 2.70) <.00001
Hypoproteinemia	3.15 (2.14, 4.63) <.00001	3.05 (2.08, 4.49) <.00001
Operation time ≥3 h	8.02 (3.64, 17.67) <.00001	8.33 (3.81, 18.20) <.00001
Laparotomy operation	2.17 (1.61, 2.93) <.00001	2.18 (1.61, 2.94) <.00001
Blood transfusion	1.44 (0.87, 2.37) .16	1.44 (1.01, 2.06) .04

TABLE 4 Sensitivity analysis results of risk factors.

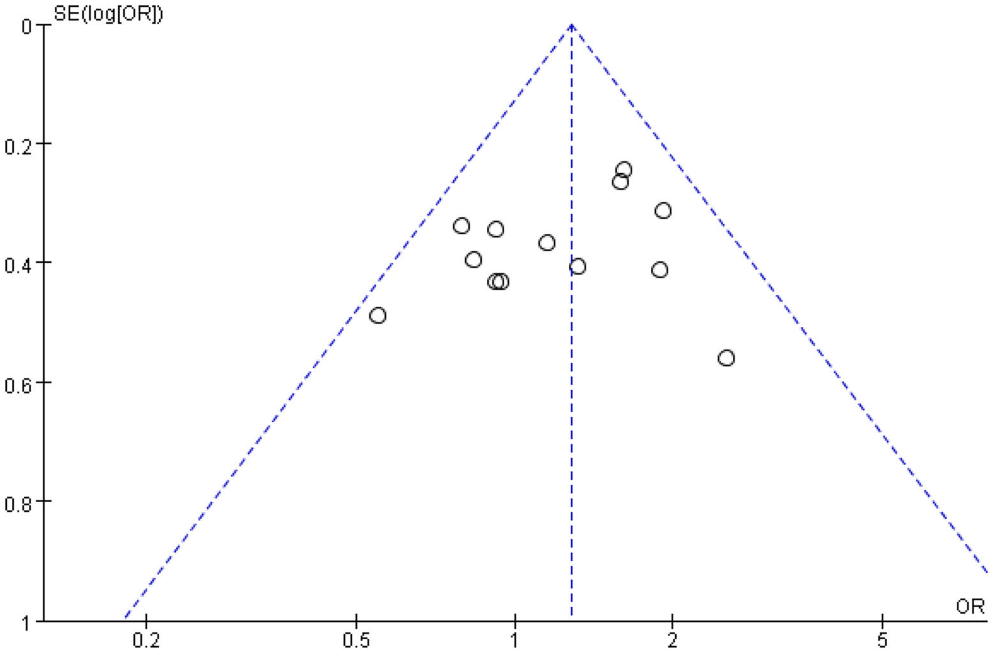

FIGURE 6 Funnel plot of sex as a risk factor.

risk screening and nutritional assessment should be performed for all gastric cancer patients, and nutritional therapy should be performed 7 to 14 days before surgery for patients with moderate to severe malnutrition and undergoing major surgery, which was beneficial to reduce SSI. Meanwhile, for malnourished patients with gastric cancer, both the American Society for Parenteral and Enteral Nutrition (ASPEN) and the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend oral/enteral feeding whenever possible.[43,44] Offering patients drink and food at will from day 1 after total gastrectomy was recommended by the ERAS consensus guidelines.[45] Therefore, in the perioperative period, the high-risk population for SSI

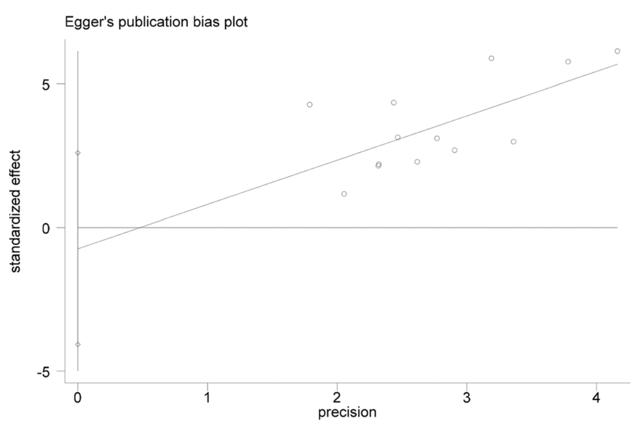

FIGURE 7 Egger plot of sex as a risk factor.

should be identified as early as possible, and individualised management should be taken to reduce the impact of disease factors on SSI, which can help promote postoperative recovery of patients.

Among the surgical operation factors, our review showed that operation time ≥3 h, laparotomy operation and blood transfusion significantly increased the risk of SSI in patients with gastric cancer. In our study, we found that operation time ≥3 h and laparotomy could increase the risk of SSI in gastric cancer patients by 8.33 times and 2.18 times, respectively, which was consistent with previous studies.[46-48] Operation time was considered to reflect complexity of the surgery[49] and it could increase the risk of SSI in gastric cancer patients by 1.52 times.[48] Inokuchi et al. also found that laparotomy surgery was associated with a significantly higher incidence of SSI than laparoscopic surgery, the former could increase the risk of SSI in gastric cancer patients by 0.5 times.[47] The prolonged operation time and laparotomy operation may lead to a prolonged period of contact between the abdominal cavity and external pathogenic microorganisms, increased intraoperative blood loss and physical trauma.[50] At the same time, blood vessels were in a state of contraction that aggravated the conditions of ischemia and hypoxia, which contributed to the increased risk of postoperative infection.[28] In our study, blood transfusion was also identified as a risk factor for the development of SSI. It had been reported that blood transfusion could cause immunosuppression and reduce the ability of anti-infection, and the risk of infection would increase by 5% with every unit of concentrated red blood cells injected.[51,52]

The limitations of this meta-analysis ought to be taken into account: (1) we included only observational studies (case–control study and cohort study) published in English or Chinese, which may lead to publication bias; (2) some risk factors were included in less literature, which may be the cause of affecting the reliability of the review results; (3) because the complete details of some exposure factors were not available, related analyses based on NRS 2002 score, body mass index, length of hospital stay, or surgical season could not be performed in this meta-analysis, which led to the loss of some information, resulting in the occurrence of reporting bias. Due to limitations in the quality and quantity of included studies, larger sample studies would be required to identify the precise indications for the above conclusions.

5 | CONCLUSION

In conclusion, this meta-analysis showed that male gender, age >60, smoking, diabetes, anaemia, preoperative obstruction, TNM ≥ III, hypoproteinemia, operation time ≥3 h, open surgery and blood transfusion were the risk factors for SSI in patients with gastric cancer. Identification of these risk factors in patients with gastric cancer would contribute to formulating relevant prevention and intervention measures to reduce the development of SSI after gastric cancer surgery.

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DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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